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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/521,264

03/08/00

GROMAN

E

1275/190

EXAMINER

HM12/0705

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ART UNIT

PAPER NUMBER

1619

DATE MAILED:

07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/521,264	Applicant(s) GROMAN ET AL.	
	Examiner Lauren Q Wells	Art Unit 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- | | |
|---|--|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 16) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 20) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Specification

The amendment filed April 23, 2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: 1) pg. 1, lines 25-26, the phrase "at doses in vast excess, for example, 100mg/kg body weight; 2) pg. 17, lines 20-21, the phrase "at higher doses; 3) pg. 19, lines 22-23, the phrase "at doses in vast excess"; 4) pg. 45, line 22, the phrase "administered in vast excess". These phrases change the scope of the invention and there appears to be no support for the amendment in the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Furthermore, the Examiner respectfully requests that in response to this objection, if the new matter is not canceled, that the Applicant points out the support for the new matter with page and line numbers in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 10-12, 14-15, 21-22, 26-30, 33-35, 37, 40, and 53-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The term "derivatized" in claims 5, 10-12, 21-22, 26-29, 35 is vague and indefinite, as it is not clear what adjustment or adjustments this term encompasses.

(ii) The term "native" in claims 14, 30, 37, is vague and indefinite, as it is not clear what this term conveys to the meaning of dextran as a chemical compound. Is native dextran, dextran? Is native dextrin reduced dextran?

(iii) The phrase "plasma extender" in claims 15, 33-34, 40 is vague and indefinite, as it is not clear what action or description this phrase is referring to.

(iv) The term "enhanced" in claim 45 (line 2) and the term "ultrasmall" in claims 53-54 (line 4) are relative terms which render the claims indefinite. The term "enhanced" and the term "ultrasmall" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 14, 16, 17, 30, 35-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Maruno et al. (5,204,457).

Maruno et al. teach a carboxyalkyl ether of a polysaccharide with a magnetic metal oxide for use as an MRI agent. Reduced dextran is disclosed as a preferred polysaccharide. Known reduction methods disclosed include a) using hydrogen in the presence of palladium carbon (a

catalyst); and b) using sodium borohydride. Carboxyalkyl ethers disclosed include carboxymethyl ether, carboxyethyl ether, and carboxypropyl ether. Iron oxide is disclosed as a preferred metal oxide. Salt forms of the complex are disclosed. The complex is disclosed as superparamagnetic. The complex is disclosed as being in the form of an aqueous sol when administered. A method of making the complex is disclosed. See Col. 1, line 39-Col. 4, line 54; Col. 5, line 44-Col. 8, line 58; Col. 11, line 10-Col. 20, line 67.

Claims 14, 16, 17, 30, 35-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Maruno et al. (6,165,378).

Maruno et al. teach a polysaccharide-magnetic metal oxide complex consisting of a polysaccharide derivative obtained by carboxyalkyl-etherifying a polysaccharide. This complex is disclosed as useful as an MRI agent. Polysaccharides disclosed include dextran and carboxyalkyl-ethers disclosed include carboxymethyl ether, carboxyethyl ether, and carboxypropyl ether. Polysaccharides are further disclosed as being reduced and being obtained by subjecting the polysaccharide to a) a method using hydrogen gas in the presence of palladium carbon; or b) a method using sodium boronhydride. Metal oxides disclosed include iron oxides. A salt form of the complex is disclosed. The complex is disclosed as being superparamagnetic. The complex is disclosed as being administered in the form of an aqueous sol. Effective doses are disclosed as being different and depending on specific purposes. A broad range of 1umol/kg-10mmol/kg is disclosed. Parenteral injection, infusion, direct enteric administration, and oral administration are disclosed as methods of administration. See Col. 1, line 44-Col. 2, line 45; Col. 5, line 37-Col. 22, line 15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maruno et al. or Maruno et al. in view of Josephson et al. (5,160,726) or Lewis (5,055,288) or Groman et al. (4,827,945) in further view of Golamn et al. (5,985,245).

Maruno et al. and Maruno et al. fail to teach autoclaving and kits (see above discussion).

Josephson et al. teach filter sterilization for production of colloidal, superparamagnetic MRI contrast agents. Disclosed is an improved method for obtaining in vivo MRI agents, wherein a colloid, which includes superparamagnetic metal oxide particles dispersed in a carrier, is sterilized prior to administration in order to avoid subjecting the active ingredient to heat stress. It is disclosed that terminal sterilization has been used with iron oxide colloids of various types, and that the resulting compounds are widely believed to have excellent toxicological properties. An example is a paramagnetic iron-dextran complex that was autoclaved prior to administration. See Col. 1, line 20-Col. 4, line 41; Col. 7, line 56-Col. 12, line 61.

Lewis et al. teach vascular magnetic imaging method and an agent comprising biodegradable superparamagnetic metal oxides. The agents are as disclosed as being autoclaved. Iron is disclosed as a superparamagnetic oxide and dextran is disclosed as a macromolecular species associated with the iron oxide. See Col. 3, line 15-Col. 9, line 35; Col. 11, line 64-Col. 16, line 31.

Groman et al. teach biologically degradable superparamagnetic materials of use in clinical applications, such as MRI. Superparamagnetic materials disclosed include iron oxides conjugated with dextran. Autoclaving solutions of superparamagnetic materials is disclosed. These complexes are disclosed as a source of nutritional iron. See Col. 2, line 30-Col. 20, line 5; Col. 26, line 32-Col. 34, line 60.

Golman et al. teach contrast agents for MRI using a manganese compound and kojic acid. Negative contrast agents disclosed for use in the composition superparamagnetic species, such as iron oxide bound with polysaccharides. A multiple container contrast agent kit is disclosed. See Col. 3, line 40-Col. 5, line 18.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the inventions of Maruno et al. or Maruno et al. using the teachings of Josephson et al. or Lewis et al. or Groman et al. and obtain a method of providing an iron oxide complex comprising the step of sterilizing the complex by autoclaving because a) Maurno et al., Maruno et al., Josehson et al., Lewis et al., and Groman et al. all teach dextran iron oxide complexes for use as MRI agents; b) Maurno et al., Maruno et al., Josehson et al., Lewis et al., and Groman et al. all teach supraparamagnetic complexes; c) Maruno et al. and Maruno et al. teach a purification step; d) Maruno et al. ('457) teach autoclaving as a means of preservation.

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Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of the combined references using the teachings of Golman et al. and obtain a kit because Golman et al. teach supraparamagnetic iron oxides bound to polysaccharides as contrast agents for use as MRI contrast agents.

The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Notes/Comments

It is noted that the term "carboxyalkylation" is spelled incorrectly in claim 6.

Prior Art

The prior art made of record and not specifically relied upon in any rejections cited above is either 1) considered cumulative to the prior art that was cited in a rejection or is 2) considered pertinent to the applicant's disclosure and shows the state of the art in its field but is not determined by the Examiner to read upon the invention currently being prosecuted in this application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana L Dudash can be reached on (703) 308-2328. The fax phone numbers for the

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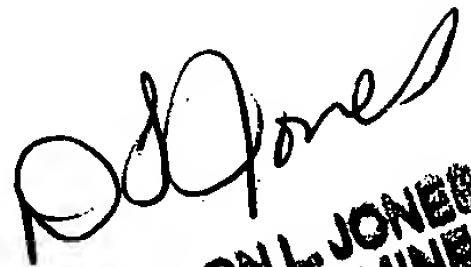
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organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
June 22, 2001


DAMERON L. JONES
PRIMARY EXAMINER